



Characteristic Needle-Shaped Pattern Seen on OCT in a Patient with Ocular Amyloidosis

Familial amyloidosis is an inherited disorder that involves amyloid deposition in various tissues and organs. The most common mutation is in transthyretin (TTR) protein, which carries thyroxine and vitamin A.¹ Transthyretin is synthesized mainly in the liver, but also in the retinal pigment epithelium and choroid plexus. Patients with amyloidosis TTR (ATTR) most frequently have neurological and cardiac involvement.² However, ocular involvement can be the presenting manifestation. This is a case report of a patient diagnosed with ATTR with ocular involvement and a characteristic OCT pattern. This is the second documented case reported of ocular amyloidosis and this OCT pattern.³

Case Report

This study was approved by the Moorfields Eye Hospital institutional review board. The protocol adhered to the tenets of the Declaration of Helsinki, and informed consent from the patient was obtained. A 69-year-old White British man sought treatment at the uveitis clinic at Moorfields Eye Hospital in March 2017 with significant bilateral visual deterioration. The patient had a history of bilateral vitritis since 2010 and previous bilateral vitrectomies. The histopathologic analysis of the left eye vitreous, obtained at vitrectomy performed in January 2012, showed fibrin clot and acellular debris, with no significant cellular fraction or malignant cells. The histopathologic analysis of the right eye vitreous, obtained at vitrectomy in March 2012, demonstrated an epiretinal membrane in the context of chronic inflammation, but no evidence of neoplasia. The patient then underwent bilateral cataract operation and yttrium–aluminum–garnet (YAG) posterior capsulotomy and experienced a few recurrences of intermediate uveitis that were managed with topical treatment alone. His medical history was significant for atrial fibrillation, pulmonary embolism, and pacemaker implantation for complete heart block, but he had no family history of amyloidosis.

At presentation, his best-corrected visual acuity, tested with a log-arithm of the minimum angle of resolution chart, was 0.60 bilaterally, and the intraocular pressure was within normal limits. Anterior segment examination showed bilateral mild anterior chamber activity, but no abnormalities were seen in the conjunctiva, cornea, iris, pupil, or trabecular meshwork. Dilated funduscopy in the right eye revealed 2 inactive parafoveal scars that had been noted previously, vitreous opacities, and blot hemorrhages in the retinal periphery. The left eye harbored an epiretinal membrane and vitreous strands. Fundus fluorescein angiography in the right eye showed vascular staining and blocking defects corresponding to retinal hemorrhages. Bilaterally, peripheral hypofluorescence, resulting from capillary nonperfusion,

was present. OCT in the right eye showed subtle thickening of the internal limiting membrane (ILM) with 2 parafoveal scars. However, in the left eye, retinal surface deposits with a needle-shaped pattern extending from the ILM to the vitreous were present (Fig 1).

Because he experienced recurrence of the vitritis, we performed another right-eye vitreous biopsy that showed eosinophil amorphous material, consistent with amyloid (Congo red staining and green birefringence), but no evidence of lymphoma or malignancy. Subsequently, we referred the patient to the National Amyloidosis Centre, where he was diagnosed with ATTR associated with the V30MTTR variant (late-onset) with cardiac involvement and small-fiber neuropathy.

Three months later, best-corrected visual acuity was 0.47 bilaterally and OCT of the left eye revealed slight progression of the previous findings. In January 2019, the patient was referred again because he had increased floaters in his left eye. On examination, no active inflammation was found, but persistent left eye vitreous strands were found, accounting for his visual symptoms. A further vitrectomy in the left eye was undertaken for visual improvement, and this was achieved. OCT of the right eye showed persistent mild ILM thickening, and OCT of the left eye showed persistent retinal surface depositions, as shown in Figures 2 and 3 (available at www.opthalmologyretina.org).

Discussion

Familial amyloidosis was described first by Andrade⁴ in 1952 in a group of patients with the ATTR changing valine at amino acid 30 to methionine (Val30Met) mutation. The amyloidogenic mutated proteins identified are TTR, apolipoprotein A-I, and gelsolin. The ATTR Val30Met is the most common mutation in the TTR gene and accounts for the substitution of methionine for valine at position 30 of protein ATTR.⁵

The most prevalent ocular manifestation in ATTR is the presence of vitreous amyloid deposits causing visual deterioration. The vitreous involvement usually is bilateral, but asymmetric.⁶ Vitrectomy may improve the visual acuity, but the amyloid deposits may recur. Other ocular features are abnormal conjunctival vessels, neurotrophic keratitis, deposits on the pupillary border and lens, glaucoma, and retinal vein occlusion.

Our patient demonstrated bilateral vitreous opacities and retinal ischemia, but no glaucoma and no conjunctival, corneal, or pupillary involvement. Bilaterally, the vitreous opacities regressed after the first vitrectomy, but recurred after some years, and the patient underwent a further vitrectomy, which gave the diagnosis of amyloidosis on histologic examination. According to a 2011 study by Beirão et al,⁷ recurrence of vitreous amyloidosis in 44 vitrectomized eyes represented no true recurrence, but rather was associated with incomplete vitrectomy.

Regarding the OCT findings, the left eye showed ILM thickening with needle-shaped deposits, presumably depicting the amyloid deposition on the retinal surface that persists after

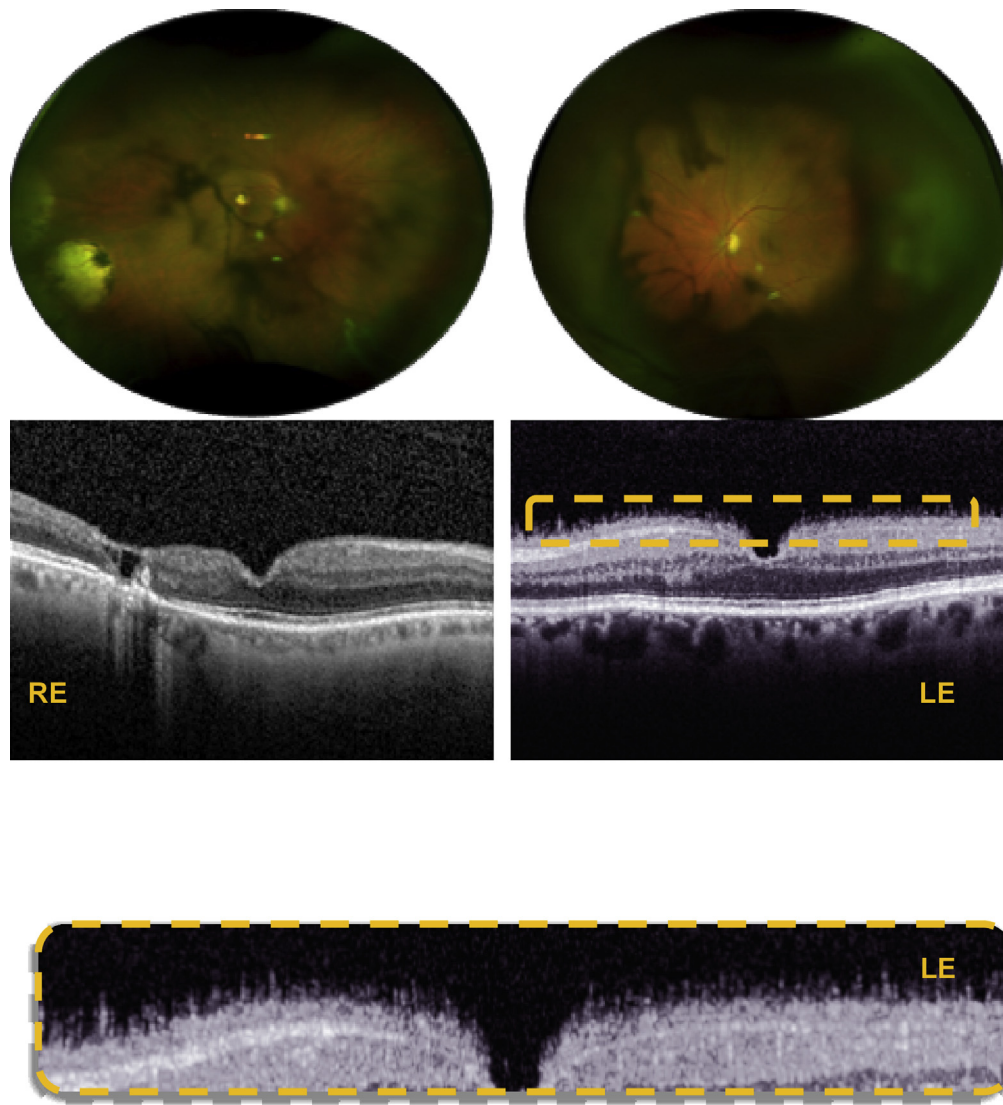


Figure 1. Fundus photographs and OCT scans from both eyes obtained in March 2017. **Top row**, Fundus photographs from both eyes showing vitreous opacities. **Second row**, OCT scans of the right eye (RE) showing mild thickening of the internal limiting membrane and of the left eye (LE) showing needle-shaped deposits on the retinal surface (yellow contour in **Second and Third row**).

vitrectomy. The right eye showed only mild ILM thickening, but not the characteristic deposits. This asymmetry between the 2 eyes may be associated with the asymmetric nature of vitreous amyloidosis^{3,6} or with incomplete vitrectomy and remaining amyloid deposits.

We decided to report this case because it is the second case described in the literature with ocular amyloidosis and this characteristic OCT pattern, identified after vitrectomy. The first case was described in 2008 by Hattori et al.³ They reported a 59-year-old patient with bilateral vitreous opacities, deposits on the pupillary border, and neovascular glaucoma, possibly associated with retinal vascular disease. His findings were asymmetric between the 2 eyes and were more prominent in the right eye. The vitreous obtained at vitrectomy of this eye showed ocular amyloidosis, and the OCT demonstrated characteristic needle-shaped amyloid deposits on the retinal surface.

In conclusion, in ocular amyloidosis, vitrectomy is the gold standard to confirm the diagnosis of vitreous involvement. However, if there are patients with this unusual OCT presentation after vitrectomy, ophthalmologists should consider amyloidosis as a differential diagnosis and should conduct further investigations because the patient may have serious organ involvement such as is seen in the heart. This OCT pattern therefore may contribute to the earlier diagnosis of ocular and systemic amyloidosis.

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No animal subjects were included in this study.

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Conception and design: Tasiopoulou, Ong, Lightman

Analysis and interpretation: Tasiopoulou, Ong, Lightman

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Abbreviations and Acronyms:

ATTR = amyloidosis transthyretin; **ILM** = internal limiting membrane; **TTR** = transthyretin; **YAG** = yttrium-aluminum-garnet.

Keywords:

Amyloid deposits on the retinal surface, Amyloidosis transthyretin changing valine at amino acid 30 to methionine mutation (Val30Met), Hereditary transthyretin amyloidosis, Needle-shaped deposits, OCT, Ocular amyloidosis, Vitreous amyloidosis.

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